National Aeronautics and Space Administration
Glenn Research Center
Cleveland, Ohio

John Glenn Biomedical Engineering Consortium
Helping Astronauts, Healing People on Earth

Microsystem for Controlled, Continuous Drug Delivery

A batteryless, potentially implantable, completely unique drug delivery system will be developed that exploits the ability of microelectromechanical systems (MEMS) technology to generate precise pore sizes on the order of the size of drug molecules. The system may allow the controlled, passive release of medicines over long periods of time, minimizing the requirements on patients.

Various pharmacological agents have been suggested as possible countermeasures to the adverse effects of microgravity on astronaut health during space exploration and habitation on the International Space Station. For example, promethazine is used to treat space sickness, while a combination of vitamin D receptor and selective estrogen receptor modulator is under investigation to maintain bone mass and strength.

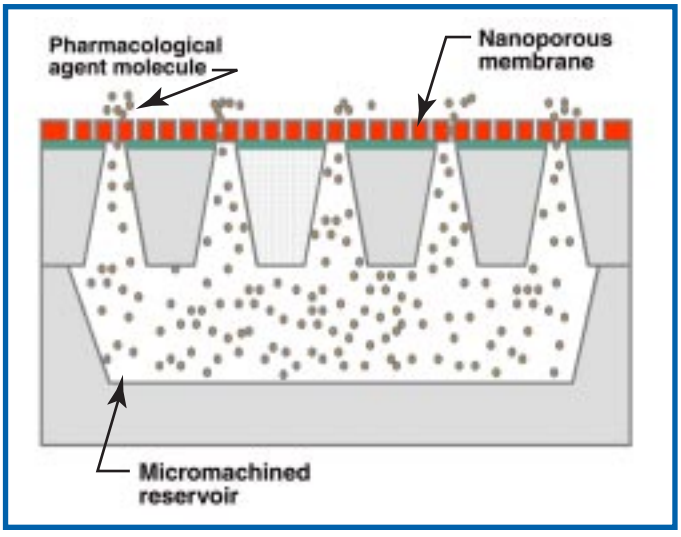
The intermittent nature of conventional administration routes such as injection and ingestion, however, is inconvenient—especially in weightlessness—and can distract astronauts from critical mission tasks. In addition, the desired therapeutic effect provided by some pharmacological agents requires continuous rather than intermittent administration.

People who take medicines on a regular basis on Earth have similar concerns: administration of drugs by injection or by mouth results in too much medication at once, or a "burst" effect, and a diminished concentration of the drug and reduced effectiveness at the end of the medication cycle. The burst effect can even be dangerous with a medication like insulin.

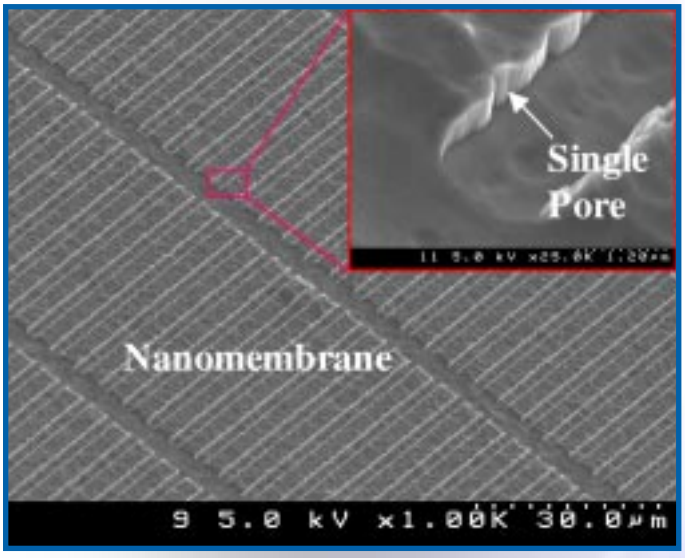
For these reasons, development of a miniature microsystem for the controlled release of drugs that could be implanted under the skin may be useful to counteract adverse effects of microgravity on astronaut health, and facilitate the administration of any needed drugs in space. For anyone taking drugs on a daily basis, an implantable microsystem could increase both the effectiveness of a medication and the confidence and freedom of the patient.

With the support of the John Glenn Biomedical Engineering Consortium (GBEC), principal investigator Shuvo Roy of the Cleveland Clinic Foundation (CCF) is collaborating with co-investigators Aaron Fleischman (CCF), David Jacqmin and Noel Nemeth (Glenn Research Center), and Christian Zorman (Case Western Reserve University) to develop a controlled-release microsystem that could be introduced into practice almost immediately to treat astronauts and to investigate various pharmacological agents at the same time.

The proposed controlled-release microsystem relies on diffusion through silicon nanomembranes, which are fabricated using microelectromechanical systems (MEMS) technology. Fluid physics and transport are critical to the action of this device. Diffusion through the nanomembrane is a function of pore size (ranging from 5 to 100 nanometers, i.e., more than 100 times smaller than the diameter of a human hair), which can be designed to achieve different rates of release. The nanomembrane will gradually release the encapsulated medicine to mimic a slow infusion, maintaining the therapeutic concentration of the drug in the patient's body.



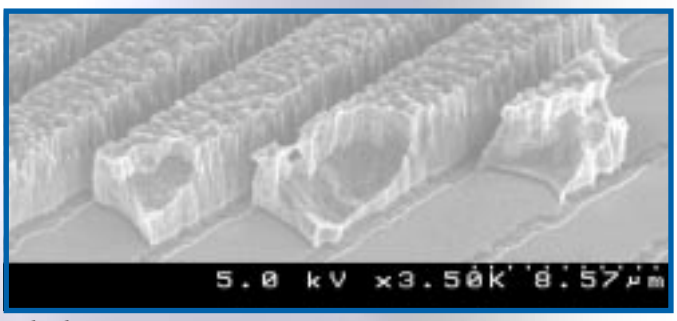
Controlled-release drug delivery microsystem.



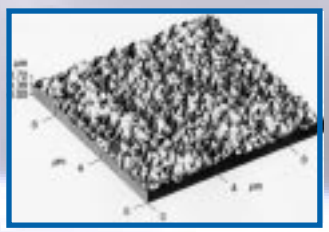
SEM image of 20 nm nanomembrane.

MEMS technology, which uses tiny micro-components that are virtually invisible to the naked eye, has enabled the creation of microsystems like this one. The feasibility of nanomembrane fabrication was demonstrated when fabrication process protocols were developed to reproducibly create 10-, 20-, 30-, 50-, and 100-nanometer-wide pores. The nanomembranes, however, were extremely fragile and susceptible to fracture upon handling. Investigations revealed that a compressive residual stress was induced in the silicon nanomembrane layers during fabrication, which caused them to buckle.

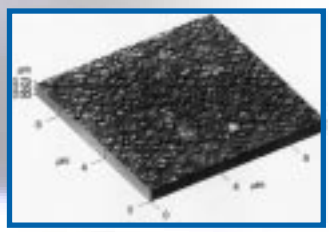
Reliability analysis will be performed that builds on work already done for MEMS pressure sensors using silicon carbide, a promising material for the fabrication of microdevices. Experimental testing, finite element analysis, and probabilistic lifing models will be used to examine stress distributions and reliability against fracture for existing designs. A predictive model will be developed to generate advanced nanomembrane designs that will be sufficiently robust to handle during testing and to withstand physiological pressures upon implantation.



Polysilicon pattern.



AFM image (615 °C growth).



AFM image (580 °C growth).

Benefits on Earth

An implantable drug delivery microsystem could very well be useful in the future for anyone who becomes sick and needs medication. Most medication works best when its administration is gradual and continuous. It is especially important to avoid the burst effect when too much medication can actually be dangerous, as with insulin. For people who need to take medication every day of their lives, this device could have a life-altering impact.

For more information about the John Glenn Biomedical Engineering Consortium or consortium projects, please contact
Marsha M. Nall
NASA Glenn Research Center
21000 Brookpark Road MS 77–7, Cleveland, Ohio 44135
grcbio@grc.nasa.gov

http://microgravity.grc.nasa.gov/grcbio

Glenn Research Center

The Research Institute
University Hospitals of Cleveland

THE CLEVELAND CLINIC FOUNDATION

CASE WESTERN RESERVE UNIVERSITY

NCMR

M–1043–09
May 02